Fibrillin 1 gene mutations in development of Tetralogy of Fallot

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Objectives: The transforming growth factor β (TGF- β) signaling has an essential role in promoting development of the heart. Fibrillin-1 (FBN1) protein interacts with latent TGF-β binding protein (LTBP-1), which is the only form expressed during embryonic development, to control TGF-β activity. The genetic cause of Tetralogy of Fallot (TOF) is heterogenous. In this report we suggested that mutations in FBN1 gene play role in development of disease in patients with TOF.

Methods: We have performed mutation detection on 26 patients with TOF from the Pediatric Cardiology Department in Dr. Sami Ulus Children's Hospital. Total RNA extracted from peripheral blood lymphocytes with the High PureRNA Isolation kit (Roche Applied Science, Indianapolis, IN) was reverse-transcribed using Transcriptor First Strand cDNA Synthesis kit (Roche Applied Science, Indianapolis, IN), according to the manufacturer's recommendations. All coding exons of *FBN1* genewere amplified with the primers described previously [10]. The polymerase chain reaction products were purified and sequenced on an ABI PRISM 3130 automated DNA sequencer (Applied Biosystems).

Results: The median age of patients was 5.8 years (range between 9 months and 17 years) and male to female ratio was 4.2. We found an FBN1 mutation detection rate of 38.4% (n:10) in patients with TOF. Seven mutations were identified, of which 6 are reported here for the first time. The detected mutation types were 1536_1538ins3,1561_1563del3 (n:1), c.6314del66ins57(n:3, 2 heterozygotes and 1 homozygote), heterozygote deletion of exon 64(n:2), heterozygote deletion of exon 57 (n:2), heterozygotep.K595E (c.1783A>G) (n:1) and heterozygote exon 13-14 deletion (n:1)

Conclusions: The mutations in FBN1 gene may be responsible for development of TOF in embryological period of cardiac development by effecting the function of long form of LTBP1L.